Agency for Healthcare Research and Quality
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NATIONAL GUIDELINE CLEARINGHOUSE

General

Guideline Title

Clinical Pharmacogenetics Implementation Consortium guideline for *CYP2D6* and *CYP2C19* genotypes and dosing of tricyclic antidepressants.

Bibliographic Source(s)

Hicks JK, Swen JJ, Thorn CF, Sangkuhl K, Kharasch ED, Ellingrod VL, Skaar TC, Muller DJ, Gaedigk A, Stingl JC. Clinical Pharmacogenetics Implementation Consortium guideline for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants. Clin Pharmacol Ther. 2013 May;93(5):402-8. [40 references] PubMed

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

The strength of therapeutic recommendations (Strong, Moderate, Optional) is defined at the end of the "Major Recommendations" field.

Genetic Test Interpretation

The cytochrome P450 2D6 (CYP2D6) activity score is used to assign phenotype in this guideline as follows: patients with an activity score of 0 are classified as poor metabolizers, those with a score of 0.5 are intermediate metabolizers, those with a score from 1.0 to 2.0 are extensive metabolizers, and those with a score >2.0 are classified as ultrarapid metabolizers (see Table 1 below and Supplementary Data in the "Availability of Companion Documents" field). Extensive metabolizers are considered to have normal CYP2D6 enzyme activity.

Table 1. Assignment of Likely Phenotypes Based on Diplotypes

Likely Phenotype	Activity Score[a]	Genotypes	Examples of Diplotypes
Assignment of CYP2D6 phenotype			
Ultrarapid metabolizer (~1–2% of patients)[b]	>2.0	An individual carrying duplications of functional alleles	*(*1/*1)xN, (*1/*2)xN, (*2/*2)xN*[c]

Likely Phenotype	Activity Score[a]	Genotypes	Examples of Diplotypes
Extensive metabolizer (~77–92% of patients)	1.0–2.0[d]	An individual carrying two functional alleles or two reduced function alleles or one functional and nonfunctional allele or one functional and reduced function allele	*1/*1, *1/*2, *2/*2, *1/*9, *1/*41, *41/*41, *1/*5, *1/*4
Intermediate metabolizer (~2–11% of patients)	0.5	An individual carrying one reduced function and one nonfunctional allele	*4/*41, *5/*9, *4/*10
Poor metabolizers (~5–10% of patients)	0	An individual carrying only nonfunctional alleles	*4/*4, *3/*4, *5/*5, *5/*6
Assignment of CYP2C19 phenotype			
Ultrarapid metabolizer (~5–30% of patients)[e]		An individual carrying two gain-of-function alleles or one functional allele and one gain-of-function allele	*17/*17, *1/*17
Extensive metabolizer (~35–50% of patients)		An individual carrying two functional alleles	*1/*1
Intermediate metabolizer (~18–45% of patients)		An individual carrying one functional allele and one loss-of-function allele	*1/*2, *1/*3
Poor metabolizers (~2–15% of patients)		An individual carrying two loss-of-function alleles	*2/*2, *2/*3, *3/*3

[a] See Supplementary Data in the "Availability of Companion Documents" field for additional information about CYP2D6 activity score and its limitations.

[b] CYP2D6 metabolizer status frequencies are based on data from Caucasians and may differ from other ethnicities.

[c] xN represents the number of CYP2D6 gene copies.

[d] Patients with an activity score of 1.0 may be classified as intermediate metabolizers by some reference laboratories.

[e] CYP2C19 metabolizer status frequencies are based on average multiethnic frequency.

Therapeutic Recommendations

CYP2D6 Dosing Recommendations

For neuropathic pain treatment, in which lower initial doses of tricyclics are used, gene-based dosing recommendations are found in the "Other Considerations" section, below. Table 2, below, summarizes the gene-based dosing recommendations for amitriptyline and nortriptyline based on CYP2D6 phenotype for situations requiring a higher initial dose, such as depression treatment. The recommended starting dose of amitriptyline or nortriptyline does not need adjustment based on genotype for CYP2D6 extensive metabolizers. A 25% reduction of the recommended dose may be considered for CYP2D6 intermediate metabolizers. Because patients with a CYP2D6 activity score of 1.0 are inconsistently categorized as intermediate or extensive metabolizers in the literature, these are difficult to evaluate, resulting in a moderate recommendation classification.

CYP2D6 ultrarapid metabolizers have a higher probability of failing amitriptyline or nortriptyline pharmacotherapy due to subtherapeutic plasma concentrations, and therefore alternative agents are preferred. There are documented cases of CYP2D6 ultrarapid metabolizers receiving large doses of nortriptyline to achieve therapeutic concentrations. However, very high plasma concentrations of the nortriptyline hydroxy metabolite

were present, which may increase the risk for cardiotoxicity. If a tricyclic is warranted, there are insufficient data in the literature to calculate a starting dose for a patient with CYP2D6 ultrarapid metabolizer status, and therapeutic drug monitoring is strongly recommended. Adverse effects are more likely in CYP2D6 poor metabolizers due to elevated tricyclic plasma concentrations, therefore, alternative agents are preferred. If a tricyclic is warranted, consider a 50% reduction of the usual dose; therapeutic drug monitoring is strongly recommended.

Table 2. Dosing Recommendations for Amitriptyline and Nortriptyline Based on CYP2D6 Phenotype

Phenotype	Implication	Therapeutic Recommendation	Classification of Recommendation
CYP2D6 ultrarapid metabolizer	Increased metabolism of tricyclics to less active compounds as compared with extensive metabolizers	Avoid tricyclic use due to potential lack of efficacy. Consider alternative drug not metabolized by CYP2D6.	Strong
	Lower plasma concentrations will increase probability of pharmacotherapy failure.	If a tricyclic is warranted, consider increasing the starting dose.[a] Use therapeutic drug monitoring to guide dose adjustments.	
CYP2D6 extensive metabolizer	Normal metabolism of tricyclics	Initiate therapy with recommended starting dose.[a]	Strong
CYP2D6 intermediate metabolizer	Reduced metabolism of tricyclics to less active compounds as compared with extensive metabolizers	Consider 25% reduction of recommended starting dose.[a] Use therapeutic drug monitoring to guide dose adjustments.	Moderate
	Higher plasma concentrations will increase the probability of side effects		
CYP2D6 poor metabolizer	Greatly reduced metabolism of tricyclics to less active compounds as compared with extensive metabolizers	Avoid tricyclic use due to potential for side effects. Consider alternative drug not metabolized by CYP2D6.	Strong
	Higher plasma concentrations will increase the probability of side effects.	If a tricyclic is warranted, consider a 50% reduction of recommended starting dose.[a] Use therapeutic drug monitoring to guide dose adjustments.	

If *CYP2C19* genotyping results are also available, see Table 3, below, for *CYP2C19*-based dosing recommendations along with Supplementary Data online (see the "Availability of Companion Documents" field). Dosing recommendations apply only to higher initial doses of amitriptyline or nortriptyline for treatment of conditions such as depression. See "Other Considerations", below, for dosing recommendations for conditions in which lower initial doses are used, such as neuropathic pain. For the dosing guidelines for clomipramine, desipramine, doxepin, imipramine, and trimipramine, see Supplementary Data online.

[a]Patients may receive an initial low dose of tricyclics, which is then increased over several days to the recommended steady-state dose. The starting dose in this guideline refers to the recommended steady-state dose.

CYP2C19 Dosing Recommendations

Dosing recommendations for neuropathic pain treatment with amitriptyline are discussed in the "Other Considerations" section, below. Table 3, below, summarizes the gene-based dosing recommendations for CYP2C19 and amitriptyline when higher initial starting doses are warranted. The usual starting dose of amitriptyline may be used in CYP2C19 extensive and intermediate metabolizers. Although CYP2C19 intermediate metabolizers would be expected to have a modest increase in the ratio of amitriptyline to nortriptyline plasma concentrations, the evidence does not indicate that CYP2C19 intermediate metabolizers should receive an alternative dose.

Patients taking amitriptyline who are CYP2C19 ultrarapid metabolizers may be at risk of having altered plasma concentrations or adverse events. Although the *CYP2C19*17* allele did not alter the sum of amitriptyline plus nortriptyline plasma concentrations, it was associated with higher nortriptyline plasma concentrations, possibly increasing the risk of adverse events. For patients taking amitriptyline, extrapolated pharmacokinetic data suggest that CYP2C19 ultrarapid metabolizers may need a dose increase. Due to the need for further studies investigating the clinical

importance of the *CYP2C19*17* allele and the possibility of altered tricyclic concentrations, the guideline authors recommend consideration of an alternative tricyclic or other drug not affected by CYP2C19. Because the clinical importance of *CYP2C19*17* is currently poorly understood, this recommendation is classified as optional. If amitriptyline is administered to a CYP2C19 ultrarapid metabolizer, therapeutic drug monitoring is recommended.

CYP2C19 poor metabolizers are expected to have a greater ratio of amitriptyline to nortriptyline plasma concentrations. The elevated amitriptyline plasma concentrations may increase the chance of a patient experiencing side effects. Consider a 50% reduction of the usual amitriptyline starting dose along with therapeutic drug monitoring.

Table 3. Dosing Recommendations of Amitriptyline Based on CYP2C19 Phenotype

Phenotype	Implication	Therapeutic Recommendation	Classification of Recommendation
CYP2C19 ultrarapid metabolizer	Increased metabolism of amitriptyline as compared with extensive metabolizers	Consider alternative drug not metabolized by CYP2C19	Optional
		If a tricyclic is warranted, use therapeutic drug monitoring to guide dose adjustments	
CYP2C19 extensive metabolizer	Normal metabolism of amitriptyline	Initiate therapy with recommended starting dose[a]	Strong
CYP2C19 intermediate metabolizer	Reduced metabolism of amitriptyline as compared with extensive metabolizers	Initiate therapy with recommended starting dose[a]	Strong
CYP2C19 poor metabolizer	Greatly reduced metabolism of amitriptyline as compared with extensive metabolizers	Consider a 50% reduction of recommended starting dose.[a] Use therapeutic drug monitoring to guide dose adjustments	Moderate
	Higher plasma concentrations of amitriptyline will increase the probability of side effects		

If *CYP2D6* genotyping results are also available, see Table 2, above, for *CYP2D6*-based dosing recommendations along with Supplementary Data online (see the "Availability of Companion Documents" field). Dosing recommendations apply only to higher initial doses of amitriptyline for treatment of conditions such as depression. See "Other Considerations", below, for dosing recommendations for conditions at which lower initial doses are used, such as neuropathic pain. For dosing guidelines for clomipramine, doxepin, imipramine, and trimipramine, see Supplementary Data online.

[a]Patients may receive an initial low dose of tricyclics, which is then increased over several days to the recommended steady-state dose. The starting dose in this guideline refers to the recommended steady-state dose.

CYP2D6 and CYP2C19 Combined Dosing Recommendations

Although specific combinations of *CYP2D6* and *CYP2C19* alleles are likely to result in additive effects on the pharmacokinetic properties of tricyclics, little information is available on how to adjust initial doses based on combined genotype information. Patients carrying at least one *CYP2D6* nonfunctional allele and two *CYP2C19* functional alleles had an increased risk of experiencing side effects when administered amitriptyline, whereas patients with at least one *CYP2C19* loss-of-function allele and two *CYP2D6* functional alleles had a low risk of experiencing side effects. Because there is only sparse clinical evidence for an additive effect of *CYP2D6* and *CYP2C19* on tricyclic dosing, the recommendations are classified as optional (see online Supplementary Data in the "Availability of Companion Documents" field).

Other Considerations

Gene-based Dosing Recommendations for Neuropathic Pain Treatment

Amitriptyline is often used at lower dosages (e.g., 0.1 mg/kg/day in pediatric patients) for treatment of neuropathic pain than when used for depressive disorders. Because of the lower dosage, it is less likely that CYP2D6 or CYP2C19 poor or intermediate metabolizers will experience

adverse effects due to supratherapeutic plasma concentrations of amitriptyline. Therefore, the guideline authors recommend no dose modifications for poor or intermediate metabolizers when prescribed amitriptyline at a lower dose for treatment of neuropathic pain, but these patients should be monitored closely for side effects. If larger doses of amitriptyline are warranted, the guideline authors recommend following the gene-based dosing guidelines presented in Tables 2 and 3, above.

Providing dose recommendations for CYP2C19 ultrarapid metabolizers when amitriptyline is prescribed at lower doses for neuropathic pain treatment is difficult. On the basis of predicted and observed pharmacokinetic data, CYP2D6 ultrarapid metabolizers are at risk of failing amitriptyline therapy for neuropathic pain, and thus alternative agents such as gabapentin should be considered. Although little information is available on how to adjust initial amitriptyline doses based on combined *CYP2D6* and *CYP2C19* genetic results when treating neuropathic pain, caution should be used when patients have a combination of poor or ultrarapid phenotypes (e.g., a CYP2D6 poor metabolizer also having CYP2C19 ultrarapid or poor metabolism).

Consideration of Drug Interactions and Patient Characteristics

Patients treated for psychiatric disorders often require multiple medications, which can influence tricyclic plasma concentrations, side effects, and therapeutic failure. For example, patients taking amitriptyline in combination with a potent CYP2D6 inhibitor, such as fluoxetine, may have dramatic increases in plasma concentrations. It has been suggested that patients taking strong CYP2D6 inhibitors should be treated similarly to CYP2D6 poor metabolizers. In addition, patients with increased age, liver disease, and reduced renal function may require reduced doses of tricyclics. Drug–drug interactions along with patient characteristics should be considered in addition to the gene-based dosing recommendations presented herein.

Minor Metabolic Pathways of Tricyclics

Other cytochrome P450 enzymes, including CYP3A4 and CYP1A2, metabolize tricyclics to a lesser extent. There is currently no strong evidence supporting gene-based dosing recommendations for other cytochrome P450 enzymes that metabolize tricyclics.

Definitions:

Strength of Therapeutic Recommendations

Strong: The evidence is high quality and the desirable effects clearly outweigh the undesirable effects.

Moderate: There is a close or uncertain balance as to whether the evidence is high quality and the desirable clearly outweigh the undesirable effects.

Optional: The desirable effects are closely balanced with undesirable effects and there is room for differences of opinion as to the need for the recommended course of action.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

- Psychiatric disorders, including depression and obsessive–compulsive disorder
- Pain, including neuropathic pain and migraine headache

Guideline Category

Prevention

Risk Assessment

Treatment

Clinical Specialty

Family Practice

Internal Medicine

Medical Genetics

Neurology

Pediatrics

Pharmacology

Preventive Medicine

Psychiatry

Psychology

Intended Users

Advanced Practice Nurses

Pharmacists

Physician Assistants

Physicians

Guideline Objective(s)

To provide information regarding how to use existing *cytochrome P450 2D6 (CYP2D6)* and/or *CYP2C19* genotyping test results to guide dosing of tricyclics for psychological disorders and pain management, focusing particularly on amitriptyline and nortriptyline

Target Population

- Patients with psychiatric disorders or neuropathic pain
- Patients requiring migraine prophylaxis

Interventions and Practices Considered

Dosing of tricyclic antidepressant therapy (amitriptyline, nortriptyline) based on *cytochrome P450 2D6 (CYP2D6)* and *CYP2C19* genotype

Major Outcomes Considered

- Rate of metabolism of tricyclic antidepressants in relation to *cytochrome P450 2D6 (CYP2D6)* and/or *CYP2C19* genotypes
- Plasma concentrations of tricyclic antidepressants in relation to *CYP2D6* or *CYP2C19* genotypes
- Side effects/adverse effects of tricyclic antidepressants in relation to *CYP2D6* or *CYP2C19* genotypes
- Treatment failure rate in relation to *CYP2D6* or *CYP2C19* genotypes

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

The guideline authors searched the PubMed® database (1966 to September 2012) for the following keywords: (cytochrome P450 2D6 or CYP2D6) OR (cytochrome P450 2C19 or CYP2C19) AND (tricyclic antidepressants OR amitriptyline OR clomipramine OR desipramine OR doxepin OR imipramine OR nortriptyline OR trimipramine) for the association between *CYP2D6* and/or *CYP2C19* genotypes and metabolism of tricyclic antidepressant drugs or tricyclic antidepressant-related adverse drug events or clinical outcomes.

The *cytochrome P450 2D6 (CYP2D6)* and *CYP2C19* allele frequency tables are based on previously published Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines. Updates to the *CYP2D6* allele frequency table were made by searching the PubMed® database (1995 to June 2012) using the following key words: CYP2D6, CYP 2D6, cytochrome P4502D6, ethnic, ethnicity, race, population, and names of countries and populations (e.g., Spain, Spanish, Brazil, Brazilian). In addition, reports were also identified from citations by others or review articles. Studies were considered for inclusion if: (1) the ethnicity of the population was clearly indicated, (2) either *CYP2D6* allele frequencies or genotype frequencies were reported, (3) the method by which *CYP2D6* was genotyped was indicated, (4) the sample population consisted of at least 50 individuals with a few exceptions (e.g., smaller cohorts that were part of larger studies) and (5) the study represented an original publication (no reviews or meta-analyses).

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Levels of Evidence

High: Evidence includes consistent results from well-designed, well-conducted studies.

Moderate: Evidence is sufficient to determine effects, but the strength of the evidence is limited by the number, quality, or consistency of the individual studies; generalizability to routine practice; or indirect nature of the evidence.

Weak: Evidence is insufficient to assess the effects on health outcomes because of limited number or power of studies, important flaws in their design or conduct, gaps in the chain of evidence, or lack of information.

Methods Used to Analyze the Evidence

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

The Clinical Pharmacogenetics Implementation Consortium (CPIC) therapeutic recommendations are based on weighting the evidence from a combination of preclinical functional and clinical data, as well as on some existing disease-specific consensus guidelines. Some of the factors that are taken into account in evaluating the evidence supporting therapeutic recommendations include: *in vivo* pharmacokinetic and pharmacodynamic data, *in vitro* enzyme activity of tissues expressing wild-type or variant-containing cytochrome P450 2D6 (CYP2D6) or CYP2C19, in vitro

CYP2D6 or CYP2C19 enzyme activity from tissues isolated from individuals of known *CYP2D6* or *CYP2C19* genotypes, and *in vivo* pre-clinical and clinical pharmacokinetic and pharmacodynamic studies. The gene-based dosing recommendations in this guideline takes into consideration the effects *CYP2D6* or *CYP2C19* genetic variants may have on both clinical outcomes and tricyclic plasma concentrations. Because the pharmacokinetic properties of tricyclic antidepressants do not differ between healthy volunteers and patients, the guideline authors evaluated pharmacokinetic data acquired from studies performed on healthy subjects and patients to assist in determining if *CYP2D6* or *CYP2C19* genetic variants affect tricyclic plasma concentrations.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

The therapeutic recommendations are simplified to allow rapid interpretation by clinicians. They have been adopted from the rating scale for evidence-based therapeutic recommendations on the use of retroviral agents found at http://aidsinfo.nih.gov/contentfiles/AdultandAdolescentGL.pdf (see the "Rating Scheme for the Strength of the Recommendations" field.

Rating Scheme for the Strength of the Recommendations

Strength of Therapeutic Recommendations

Strong: The evidence is high quality and the desirable effects clearly outweigh the undesirable effects.

Moderate: There is a close or uncertain balance as to whether the evidence is high quality and the desirable clearly outweigh the undesirable effects.

Optional: The desirable effects are closely balanced with undesirable effects and there is room for differences of opinion as to the need for the recommended course of action.

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Peer Review

Description of Method of Guideline Validation

Not stated

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The evidence summarized in Supplemental Tables S12-18 (see the "Availability of Companion Documents" field) is graded using a scale based on previously published criteria and applied to other Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines (see the "Major Recommendations" field). Every effort was made to present evidence from high-quality original research studies. In addition, the guideline authors took into consideration all available peer-reviewed published literature including other gene-based dosing recommendations.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

For patients who have existing *cytochrome P450 2D6 (CYP2D6)* and/or *CYP2C19* genotyping test results, the potential benefit is identifying those patients who are at an elevated risk of experiencing side effects or therapeutic failure. For those patients, dose adjustments can be made or an alternative agent selected.

Potential Harms

- A limitation inherent to most commercially available genotyping tests is that rare or *de novo* variants are not detected. In addition, some alleles are not well characterized, resulting in uncertainty when predicting the phenotype for some genetic test results. Genotyping is reliable when performed in qualified reference laboratories, but, as with any laboratory test, an error can occur. Any errors in genotyping or phenotype prediction, along with the presence of a rare genomic variant not tested for, could potentially affect the patient lifelong.
- Tricyclics are associated with multiple adverse effects, which can cause patients to fail therapy. Common adverse effects include anticholinergic, central nervous system, and cardiac effects. Tertiary and secondary amines along with their metabolites have unique side-effect profiles as detailed in the Supplementary Data online (see the "Availability of Companion Documents" field).

Qualifying Statements

Qualifying Statements

Caveats: Appropriate Use and/or Potential Misuse of Genetic Tests

The application of genotype-based dosing is most appropriate when initiating therapy with a tricyclic. Obtaining a pharmacogenetic test after months of drug therapy may be less helpful in some instances, given that the drug dose may have already been adjusted based on plasma concentrations, response, or side effects. Similar to all diagnostic tests, genetic tests are one of several pieces of clinical information that should be considered before initiating drug therapy.

Disclaimer

Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines reflect expert consensus based on clinical evidence and peer-reviewed literature available at the time they are written; they are intended only to assist clinicians in decision making and to identify questions for further research. New evidence may have emerged since the time a guideline was submitted for publication. Guidelines are limited in scope and are not applicable to interventions or diseases not specifically identified. Guidelines do not account for all individual variations among patients and cannot be considered inclusive of all proper methods of care or exclusive of other treatments. It remains the responsibility of the health-care provider to determine the best course of treatment for a patient. Adherence to any guideline is voluntary, with the ultimate determination regarding its application to be made solely by the clinician and the patient. CPIC assumes no responsibility for any injury to persons or damage to persons or property arising out of or related to any use of CPIC's guidelines, or for any errors or omissions.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

Hicks JK, Swen JJ, Thorn CF, Sangkuhl K, Kharasch ED, Ellingrod VL, Skaar TC, Muller DJ, Gaedigk A, Stingl JC. Clinical Pharmacogenetics Implementation Consortium guideline for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants. Clin Pharmacol Ther. 2013 May;93(5):402-8. [40 references] PubMed

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2013 May

Guideline Developer(s)

Clinical Pharmacogenetics Implementation Consortium - Independent Expert Panel

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Guideline Committee

Not stated

Composition of Group That Authored the Guideline

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The authors declared no conflict of interest.

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available from the Pharmacogenomics Knowledgebase Web site .

Availability of Companion Documents

The following are available:

- Supplementary material, including tables and methodological information, is available from the Pharmacogenomics Knowledgebase Web site .
- An interactive dosing table is available from the Pharmacogenomics Knowledgebase Web site .
- "Look up" tables by gene, which contain phenotype and clinical support system information based on haplotypes and diplotypes, are available from the Pharmacogenomics Knowledgebase Web site .

Patient Resources

None available

NGC Status

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